## Spatial Quantification of Intramuscular Fat Clustering Reveals Age-Related Differences in Human Ankle Extensor Muscles

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# **Summary**

Accumulation of intramuscular fat (IMF) is an important marker of skeletal muscle health, with the spatial distribution of IMF proposed to influence muscle function and to be a potential novel biomarker of neuromuscular disease progression. Three-dimensional intramuscular fat fraction (FF) distribution was reconstructed from Dixon MRI to quantify the spatial characteristics of IMF in the ankle extensor muscles of young and older adults. The results showed more branch-like patterns and clustered intramuscular FF with aging.

### Introduction

IMF refers to the adipose tissue located within skeletal muscles, often accumulating as part of the natural aging process or as a result of pathology. Previously, IMF has been assessed with quantitative MRI methods by reporting the mean FF values in specific muscle regions or along the entire muscle length [1, 2]. However, the mean FF is a summary measure. It does not provide any indication of the spatial distribution of the FF within the skeletal muscle such as whether it is densely clumped or more sparsely scattered. Based on the modelling work from Rahemi et al [3], different IMF patterns could significantly influence muscle function. Therefore, in order to quantify FF spatial properties and improve our understanding of age-related muscle weakening, here we introduce a method to quantify intramuscular FF distribution throughout the muscle volume in FF-MRIs.

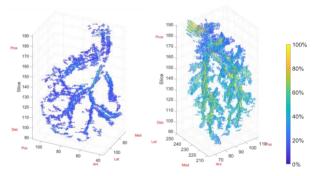
#### Methods

Nineteen young (7 females, 12 males;  $23.8 \pm 3.6$  years) and 13 older (5 females, 8 males;  $70.1 \pm 2.2$  years) healthy and physically active adults were included in the study. T1-weighted and m-Dixon images of the dominant leg were collected with 3T MRI (Magnetom Prisma, Siemens). FF images were used to quantify intramuscular FF within MG, LG, and SOL muscles. An automatic seed point-based regiongrowing method was developed to extract the voxels regarded as intramuscular FF voxels in the FF images. Extraction was based on the distribution of FF values within the muscle volume. Delaunay tessellations and Ripley's functions were used to quantify the spatial properties of intramuscular FF.

## **Results and Discussion**

In general, 3D intramuscular FF distribution showed distinct differences in the patterns observed between different ages

(Figure 1). In older participants, the intramuscular FF voxels appeared more densely clustered with an increased number of branch-like structures compared to young participants. Smaller metrics from Delaunay tessellations were found for both the mean edge length (p < 0.001) and mean volumes (p< 0.001) in older participants, indicating denser intramuscular FF distribution with smaller gaps between FF clusters. From the Ripley's K function, higher peak K values were observed for the older participants, again suggesting more intramuscular FF clusters. The age-related differences could be attributed to muscle fiber atrophy, the voids left by deteriorating muscle tissue are likely filled with IMF, leading to a denser spatial distribution. This more tightly clustered IMF can be qualitatively linked to reduced muscle function and contractile efficiency, compromising whole muscle force production capability.



**Figure 1**: 3D intramuscular FF patterns for MG muscle from a young (left sub-image) and older (right sub-image) participants.

### **Conclusions**

This study provides the first detailed quantification of the three-dimensional distribution of intramuscular FF across the ankle extensor muscles in healthy young and older adults, revealing significant variations with aging. The approach can be used to provide valuable insights into the processes of muscle degeneration with aging.

## Acknowledgments

We thank the UQ Centre for Advanced Imaging for their support and expertise in MR imaging.

### References

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